Electrochemotherapy immune response enhancement by gene electrotransfer using IL-2 and IL-12 genes in canine patients

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Introduction: Electrochemotherapy (ECT) is a treatment strategy which has been gaining territory since the publication of the ESOPE study in 2006. The immune response elicited by ECT is well documented, in fact it is the key to the high response rates obtained by the treatment, but it is ineffective against distant metastasis and also there are some tumors that are non-responding. This could be due to the fact that humoral immune response is elicited instead of cellular response, being the last one much more effective against distant metastasis. We propose the combination of ECT and gene electrotransfer (GET) in order to enhance the immune response and switch it from humoral to cellular type.

Patients and methods: Five canine patients with an ECT non-responding tumor were selected regardless of its histology. The patients were treated with ECT, followed by GET using canine IL-2 and IL-12 genes injected in the periphery of the tumor and in the quadriceps muscle. The aim of this strategy is to increase the local immune response through local IL-2 production, and to switch it from humoral to cellular through the IL-12 production at systemic level. After the treatment, the patients were followed for 6 months so far.

Results: Side effects were fever, swelling of the transfection sites and lethargy, that resolved with corticosteroid treatment during the first week. In four cases the lesions evaluated stopped growing and remained stable up to now. The fifth case had lung metastasis which reduced their size being undetectable in the control chest radiograph.

Conclusion: Our preliminary data show that ECT and GET can be safely and successfully combined. This approach can enhance the immune response in ECT non-responding tumors. Further research is being performed to assess the specific role of GET in combination with ECT treatment.